# Chemical, Bacteriological, and Toxicological Properties of Cyanuric Acid and Chlorinated Isocyanurates as Applied to Swimming Pool Disinfection

# **A Review**

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The literature on chemical and bactericidal properties and toxicity of cyanuric acid and chlorinated isocyanurates is reviewed. Experiments on rats and mice are reported and discussed. Further research is proposed.

# Introduction

Since 1958 cyanuric acid and cyanurates have been used in swimming pool water to lower the rate of photochemical reduction of chlorine, hypochlorous acid, and hypochlorite ion. Such increase of stability of chlorine to sunlight is highly desirable because it reduces both the possibility of disinfection failures and the frequency of additions of disinfectant. Chlorinated isocyanurates, pure or in commercial preparations, are also available for use as disinfectants in swimming pool water.

In this paper, the available literature is examined to

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determine (1) the influence of cyanuric compounds on the bactericidal activity of chlorine and the effectiveness of chlorinated isocyanurates as swimming pool disinfectants; (2) the acute and chronic toxicity of cyanuric acid, chlorinated isocyanurates, and their eventual decomposition products; and (3) the practical range of optimum concentrations of cyanuric acid as a chlorine stabilizer in pool water.

# Physicochemical Properties

Cyanuric acid and its derivatives are heterocyclic compounds of the symmetric triazine group (Figure 1). The predominant tautomeric form in the solid state is the keto form; in basic solution, the enol form is more stable. The synthesis and properties of cyanuric acid and its derivatives have been described in detail.<sup>1-9</sup>

The most common chlorinated isocyanurates used as swimming pool disinfectants are dichloro and trichloro

s - Triazine

Cyanuric acid or 2,4.6-s-triazinetriol

Isocyanuric acid or 2,4,6 (1H,3H,5H)s-triazinetrione

figure 1 Tautomeric forms of cyanuric acid.

derivatives such as dichloroisocyanuric acid, or 2,4,6-(1H,3Cl,5Cl)-s-triazinetrione; sodium dichloroisocyanurate, or 2,4,6-(1Na,3Cl,5Cl)-s-triazinetrione; and trichloroisocyanuric acid, or 2,4,6-(1Cl,3Cl,5Cl)-s-triazinetrione. These compounds are usually prepared by controlled chlorination of sodium or potassium salts of cyanuric acid:

$$Na_3 C_3 N_3 O_3 + 2Cl_2 \longrightarrow NaCl_3 C_3 N_3 O_3 + 2NaCl_3 C_3 N_3 O_3 N_3 O_3 + 2NaCl_3 C_3 N_3 O_3 N_$$

Some commercial formulations contain additives such as Ag<sub>3</sub>PO<sub>4</sub> to stabilize and deodorize the active product.<sup>10</sup>

In concentrated solutions of dichloro- and trichloro-isocyanurates (concentration > 0.5 per cent available chlorine), appreciable ring decomposition may be experienced. When trichloroisocyanuric acid is used, one of the products of the decomposition is  $NCl_3$ , which is a strong lacrimator and a dangerous explosive if ignited by a spark. In concentrations below 1,000 ppm as available chlorine decomposition of dichloro and trichloro derivatives in the pH range 3-14 is slow, and the nitrogen decomposition products are  $N_2$  (at pH 8.5-14) or  $N_2$  +  $NCl_3$  (at pH 3-8.5).

# **Identification and Quantitative Determination**

Numerous analytical methods have been proposed and developed for the qualitative and quantitative determination of cyanuric compounds. Effective spectrophotometric procedures, based on the intense ultraviolet light absorption of cyanuric structures in the 215- to 260-nm region are suggested by Boitsov and Finkel'Shtein<sup>11</sup> and Masayoshi. 12

Melamine reacts at pH 5.8 with cyanuric acid, yielding an insoluble, chemically defined compound containing 50.58 per cent of cyanuric acid. This reaction is used for the gravimetric determination of cyanuric acid, melamine, and chlorinated isocyanurates (after treatment with sodium arsenite to remove chlorine<sup>6</sup>, <sup>13</sup>) and is used also in a turbidimetric modification of this method which is particularly suitable for field applications.<sup>6</sup>

Acid-base titration procedures<sup>6</sup> and a method for continuous separation, identification, and quantitative determination of cyanuric acid in aqueous solutions by ion exclusion-partition chromatography<sup>14</sup> are also available.

# Handling and Storage

Cyanuric acid and cyanurates should be stored in a dry, cool place, and contact with eyes or ingestion must be prevented. Because of the possibility of explosion, manufacturers' instructions should be followed scrupulously when handling chlorinated isocyanurates.

# Stabilization Effect

The effectiveness of cyanuric acid as a chlorine stabilizer at pH 7.0 in distilled water and chlorine-demand-free pool water is shown in Table 1. Concentrations of cyanuric acid in the range from 20 to 25 ppm seem the most practical, since little is gained with a higher concentration of stabilizer. The effect of pH is shown in Table 2. Although some differences of behavior in buffered distilled water and in pool water are evident, the optimum pH for chlorine stabilization in swimming pool water is near 7.0.

While the general stabilizing properties of cyanuric acid and cyanurates are agreed upon, the basic mechanism of chlorine stabilization is unknown. When, as in swimming pool water, the molar ratio of cyanuric acid to chlorine is high, a mono-N-chloro derivative, which is more stable to ultraviolet radiations than chlorine, may be formed.

# Influence on Chlorine Bactericidal Activity

Numerous investigators have evaluated the effect of cyanuric acid on the bactericidal action of chlorine under laboratory and swimming pool conditions.

#### LABORATORY INVESTIGATIONS

Experiments on standard test organisms with various forms of chlorine in distilled water, with and without phosphate buffering, led to the conclusion that cyanuric acid and cyanurates decrease the bactericidal activity of chlorine.<sup>15,16</sup> The increase in free chlorine necessary to offset the effect of cyanuric acid is shown in Table 3.

In the absence of cyanuric acid, the pH value determines the chlorine activity, since it defines the relative

concentration of the form HClO in aqueous solutions of inorganic hypochlorites according to

and since the germicidal activity of the acid form HClO is approximately 100 times that of the base form ClO<sup>-.16</sup> However, the pH has no remarkable effect when cyanuric acid is present in the system. In fact, in the presence of 50 mg per liter of cyanuric acid, an initial concentration of available residual chlorine of 0.602 mg per liter does not produce a 99.999 per cent inactivation of *Streptococcus faecalis* in 2 min, or of *Escherichia coli* in 30 sec, even if the pH is kept as low as 5.7.<sup>16</sup> In the absence of cyanuric acid, a free chlorine concentration of 0.11 mg per liter is adequate at pH 7.2.<sup>15</sup> The cause of such behavior is probably found in the existence of multiple equilibria among organic and inorganic forms of chlorine (Figure 2).

TABLE 1—Effect of Cyanuric Acid on the Stability of Hypochlorite Solutions Exposed to Sunlight at pH 7.0\*

	% Ch	lorine F	Remainir	ng after	Exposu	re for
	1 hr	2	hr	3	hr	7 hr
Cyanuric Acid						
(ppm)	Α	Α	В	Α	В	В
0	25	10	37	5	15	0
5	54	41		38		
10	65	54		52		
20	75	67		63		
25	77	71	92	66	84	48
30	78	72		68		
100	82	77	94	74	89	68

<sup>\*</sup> Approximate values from a graph by Nelson.<sup>6</sup> Used by permission. A = Chlorine-demand-free pool water,  $29-32^{\circ}$  C, partly cloudy day; initial (OCI)<sup>-</sup> concentration, 2.5 ppm. B = Chlorine-demand-free water, sunny day,  $30-35^{\circ}$  C; initial concentration, (OCI)<sup>-</sup>, 2-3 ppm.

TABLE 2-Effect of pH on the Stability of Hypochlorite Solutions to Sunlight in Presence of 50 ppm Cyanuric Acid\*

	% C	hlorine Re	emaining at	fter Exposur	e for	
	1 hr	2	hr	4 hr	7 hr	
рН	Α	Α	В	В	В	
5	62	45	76	52	32	
6	83	79	88	78	62	
7	94	90	88	82	74	
8	88	83	84	69	48	

<sup>\*</sup> Approximate values derived from a graph by Nelson.<sup>6</sup> Used by permission. A = Chlorine-demand-free pool water, 3,000-11,000 ft-candles,  $33-36^{\circ}$  C; initial (OCI)<sup>-</sup> concentration, 3 ppm. B = Chlorine-demand-free water, 7,000-11,000 ft-candles,  $33-36^{\circ}$  C; initial (OCI)<sup>-</sup> concentration, 3 ppm.

TABLE 3-Concentrations of Free Available Residual Chlorine (mg per Liter) Needed to Obtain 99.999 per cent Inactivation of Selected Organisms with and without Cyanuric Acid (25° C, pH 7.2, Alkalinity 50 mg per Liter)\*

	-		Source of Residual Chlorine			
Test Organism	Time of Expo- sure	Cyanuric Acid (mg/ Liter)	Calcium hypo- chlorite	Trichlo- roisocy- anuric acid	Potassium dichloro- isocy- anurate	
E. čoli	30 sec	0.0	<0.11	<0.11	<0.11	
		50.0	0.97	0.80	>0.80	
S. faecalis	2 min	0.0	<0.10	< 0.11	0.11	
		50.0	0.51	0.42	0.43	
S. aureus	5 min	0.0	< 0.40	< 0.61	0.64	
		50.0	1.64	>0.90	>1.62	

<sup>\*</sup> From Robinton and Mood. 15 Used by permission. A 99.999 per cent reduction of *E. coli* in 30 sec and of *S. faecalis* in 2 min is the criterion used by the Pesticides Regulation Division, Agricultural Research Service, U.S. Department of Agriculture, in evaluating the bactericidal effectiveness of disinfectants recommended for use in swimming pool water. 15

The lower pH would have no marked effect on bactericidal activity because HClO is utilized to form an N-chloro derivative more stable to sunlight reduction but less active than HClO.

# FIELD INVESTIGATIONS

Field evaluation of the effect of cyanuric acid and cyanurates on the bactericidal action of chlorine in swimming pools is difficult because of uncontrolled or uncontrollable variables, including the daily numbers of bathers per unit volume of water, the cleanliness index of the pool, the type and efficiency of filtration, and the quantity of contaminants.

Kowalski and Hilton<sup>17</sup> analyzed data concerning the disinfection of public, semipublic, and private pools in St. Louis County, Missouri, during the 1960 and 1963 seasons. In 1960 no statistically significant difference was found in the incidence of disinfection failures between outdoor pools chlorinated with and without cyanuric acid, whether large public pools or small semipublic pools. But in two public indoor pools (Table 4) the bactericidal activity of chlorine appeared to be increased by the presence of cyanuric acid.

Other investigators, however, report cases of inhibition of chlorine activity in the presence of cyanuric acid in swimming pool water under usual conditions of operation. Donohue and Mulligan observed an unsatisfactory disinfection in eight pools operated for 9 weeks at pH 7.7–9.0 in the presence of 1.0–1.5 mg per liter of free available chlorine and 15–50 mg per liter of cyanuric acid. In this case, the relatively high pH might explain the unsatisfactory results.

The contradictory reports from field investigations

suggest that swimming pool water may contain other agents that interfere with chlorine's bactericidal activity. The influence of normal and occasional components of swimming pool water on the bactericidal properties of the chlorine and chlorine plus cvanuric acid systems should be investigated. Fitzgerald and DerVartanian20 report that the presence of 100 mg per liter of cyanuric acid in solutions of 0.5 mg per liter chlorine (free available chlorine concentration before addition of ammonia-nitrogen) and 0.075-0.5 mg per liter ammonia-nitrogen in buffered distilled chlorine-demand-free water, pH 7.3, reduced considerably the time for 99.9 per cent inactivation of S. faecalis (106 per ml). Similar results were obtained with unfiltered or membrane-filtered swimming pool water to which 0.3 mg per liter ammonia-nitrogen had been added. This was presumably due to the presence of a monochloro derivative of cyanuric acid, which is a more effective disinfectant than chloroamines.

Bactericidal Effect of Chlorinated Isocyanurates

# LABORATORY INVESTIGATION

Robinton and Mood<sup>15</sup> found no significant difference in the bactericidal activity of calcium hypochlorite, trichloroisocyanuric acid, and potassium dichloroisocyanurate when the concentration of these compounds was

**figure 2** Probable equilibria in aqueous solutions of hypochlorites and cyanuric acid under swimming pool conditions.

expressed as free available chlorine and *E. coli* and *S. faecalis* were used as test organisms. To obtain the same rate of killing of *Staphylococcus aureus*, however, a concentration of chlorinated isocyanurate as free available chlorine slightly higher than the concentration of hypochlorite was required. Cyanuric acid (50 mg per liter) reduced the effectiveness of all three sources of chlorine, but the combination of trichloroisocyanuric acid plus cyanuric acid was somewhat more effective (Table 3).

# FIELD INVESTIGATION

Kowalski and Hilton<sup>17</sup> found that pools treated with chlorinated isocyanurates have a better disinfection record than pools treated with chlorine gas or calcium hypochlorite. The authors postulate that this is due to stabilization of the residual chlorine level by cyanuric acid.

# Toxicity of Cyanuric Compounds

# Acute, Oral Toxicity

Reports on the acute, oral toxicity of cyanuric acid, monosodium cyanurate, and some chlorinated isocyanuric derivatives (Table 5) show LD<sub>50</sub> values for rats of 0.75 gm per kg and higher. A swimmer who weighs 50 kg and ingests 100 ml of water containing 25 mg per liter of cyanuric acid and 3.5 mg per liter of trichloroisocyanuric acid (about 3.1 ppm available chlorine) receives less than 1/100,000 of the LD<sub>50</sub> of either compound.

# **Chronic Toxicity**

# CYANURIC ACID AND CYANURATES

Oral daily administration of 30 mg of cyanuric acid per kg of body weight to guinea pigs and rats for 6 months

TABLE 4-Disinfection Records of Two Indoor Public Swimming Pools Chlorinated with and without Cyanuric Acid\*

			Average Conditions in Pools†				Disir	% nfection ilures
Pool Code	Source of Chlorine	No. of Tests	Chlorine (ppm)	рН	Bather Ioad‡	Cyanuric acid (ppm)	Plate count ≥200	E. coli >0
G	Chlorine gas with cyanuric							
G,	acid Chlorine	22	0.6 ± 0.5	7.2 ± 0.5	2.2 ± 2.0	33 ± 25	24	0
<b>-</b> 1	gas	9	0.9 ± 0.3	7.1 ± 0.3	2.2 ± 0.8	0	66	22

<sup>\*</sup> Prepared with data reported by Kowalski and Hilton.<sup>17</sup> Original title of table: "Summary of Results, 1960 Swimming Pool Tests, St. Louis County, Mo." Used by permission.

<sup>† 95%</sup> confidence limits.

<sup>‡</sup> Daily average number of bathers per 1,000 gallons.

TABLE 5—Acute, Oral Toxicity of Cyanuric Acid, Monosodium Cyanurate, and Some Chlorinated Isocyanuric Compounds

Cyanuric Compound	LD <sub>s o</sub> for Rats* (gm/kg)
Cyanuric acid	>5.00†
Monosodium cyanurate	>7.50†
Sodium dichloroisocyanurate	1.67‡
Potassium dichloroisocyanurate	1.22‡
Trichloroisocyanuric acid	0.75‡

<sup>\*</sup>  $LD_{5.0}$ , Minimum dose which is lethal to 50 per cent of test animals.

† Source: Mazaev.<sup>2</sup> 2 ‡ Source: FMC Corp.<sup>30</sup>

caused dystrophic changes in their kidneys, but daily doses of 3.0 mg per kg of cyanuric acid or 10 mg per kg of monosodium cyanurate apparently had no adverse effect.<sup>21,22</sup>

A renal effect was also observed by Hodge et al.,<sup>23</sup> who fed 20 male and 20 female rats for 20 weeks a diet containing 8 per cent monosodium cyanurate. Fourteen males and four females died during the experimental period. Autopsy showed histological changes in the kidneys, probably related to the diuretic effect of cyanuric acid: the distal collecting tubules and Bellini's ducts were dilated, with focal areas of epithelial proliferation. In a parallel experiment, however, a diet containing 0.8 per cent of monosodium cyanurate caused no pathological effect or toxic symptoms.

In a 2-year study by the same group<sup>2 3</sup> a diet containing 8 per cent of monosodium cyanurate was given daily to three dogs. Two dogs died after 16 months and 21 months on the regimen, and microscopic examination revealed kidney fibrosis, focal dilation, and epithelial proliferation of Bellini's ducts. Autopsy of the third dog, sacrificed after 2 years, showed the same renal changes plus atrophy of the thyroid, with lymphocytic infiltration but without evidence of hyperplasia. A diet containing 0.8 per cent of monosodium cyanurate, however, given to three dogs for 6 months caused no evident adverse effects. Organ weights and kidney tissues were normal, and the thyroids were not enlarged.

# CHLORINATED ISOCYANURATES

Hodge<sup>24</sup> found no toxicity to rats and dogs from sodium dichloroisocyanurate, one of the chloro derivatives of cyanuric acid most commonly used to disinfect swimming pool water. Hematological values, urinary sugar and protein, body weight increase, organ weights, and histological appearance of tissues did not reveal toxicity resulting from the administration for 6 months of diets containing 16.6 and 333 ppm of this compound.

# Carcinogenic Effects

A low blastomogenic effect in rats and mice, with tumors appearing after latent periods of 18 months or longer, has been attributed by Pliss and Zabezhinskii to the administration of cyanuric acid.<sup>25</sup> Apparently without contemporary controls, the compound was applied subcutaneously, orally, and topically to groups of 50 animals as follows.

#### **ORAL ADMINISTRATION**

Cyanuric acid was fed in the diet to rats and mice, 5 days per week, in daily doses of 150-300 and 280-310 mg per kg of body weight, respectively. Among the rats, the first tumor (a cysticerian sarcoma) appeared in the 19th month in one of the 30 survivors. Similar neoplasms were observed in four more rats between 21.5 and 25 months. Two cases of fibroadenoma of the mammary glands (probably spontaneous) were diagnosed in two females. Among the mice, two cases of myeloid leukosis were observed in the 23rd month. At the appearance of the first tumor, 14 animals had survived.

# **DERMAL APPLICATIONS**

Two or three drops of a 20 per cent cyanuric acid solution in benzene were smeared onto the skin of the mice three times per week. Tumors of the liver (one case of cavernous hemangioma and one case of adenoma) were observed in two survivors in the 23rd and 25th months. When the first tumor was diagnosed, eight animals were still living.

# SUBCUTANEOUS INJECTIONS

Rats and mice received weekly injections of 300-600 and 550-620 mg of cyanuric acid in sunflower oil per kg of body weight, respectively. Among the rats, one case of lung lymphosarcoma was observed in the 28th month in one of the five survivors. A subdermal lipoma was found in one of the survivors 30.5 months after the first injection. No tumors were observed among the mice.

# **Embryotoxic Effects**

# TERATOGENIC EFFECTS IN ALBINO RATS

In two studies<sup>26,27</sup> groups of 19 females were given orally via gavage single daily doses (500 mg per kg of body weight) of monosodium cyanurate with or without 36 mg of calcium hypochlorite\* in distilled water from the 6th through the 15th day of gestation. Maternal body weights and mortality were recorded throughout the investigation. On the 20th day of gestation all females were sacrificed by

<sup>\*</sup> Commercial product containing 70 per cent active chlorine.

CO<sub>2</sub> asphyxiation. Implantation and resorption sites, corpora lutea, and viable fetuses were counted and examined. External abnormalities and the skeletal and internal development of fetuses were also recorded. In both investigations, no significant differences concerning the above parameters were observed between test and control groups.

# MUTAGENIC EFFECTS IN ALBINO MICE<sup>28</sup>

Groups of 12 males each received intraperitoneal injections of a single dose (250 mg per kg of body weight) of monosodium cyanurate with or without 16.8 mg of calcium hypochlorite\* in warm distilled water. Each male was placed in a breeding cage with three virgin females. Each week and for 6 consecutive weeks the females were replaced with another group of three females. Males and females were sacrificed by CO<sub>2</sub> asphyxiation at the end of the 6-week mating period and 1 week after removal from the cage, respectively. Neither treatment induced a dominant lethal response. No significant differences were observed between test and control groups concerning implantation and resorption sites, embryos, or mutation rates.

#### **Short Term Investigations**

# **ORAL ADMINISTRATION**

In a 1-month study by Hodge,<sup>29</sup> groups of five male rats were given drinking water containing 400, 1,200, 4,000, and 8,000 ppm of trichloroisocyanuric acid (as available chlorine). These solutions, after addition of NaOH to adjust pH to 7.2—7.6, were aged 3 to 4 days before use.

Access to the water supply was unrestricted, and new solutions were offered every 3 to 4 days. In the first week the rate of weight increase was reduced at all concentrations of the compound by voluntary reduction of water intake, probably due to the disagreeable odor and taste of the solutions. Thereafter, both water intake and growth rate of the rats on the 400-, 1,200-, and 4,000-ppm diets increased; their growth rate approached that of the control rats in the second and third weeks of the treatment.

Throughout the entire experimental period, the water intake and growth rate of the rats given the 8,000-ppm solution remained markedly lower than those of the control rats. One rat given the 4,000-ppm solution died. However, the organs of the rats on the 4,000- and 8,000-ppm diets appeared normal under gross pathological examination.

In another experiment by Hodge,<sup>29</sup> groups of five male rats were given tap water containing trichloroisocyanuric acid (2, 10, and 20 ppm as available chlorine) and cyanuric acid in a 1:200 concentration ratio. These solutions were treated and administered for a month as in the preceding study. Here also the growth rate was somewhat reduced but the effect was not concentration-dependent. No rats died during the experimental period, and autopsy of those given the highest concentrations revealed no organ abnormalities under gross examination.

# **Topical Applications**

# **TESTS ON ALBINO RABBITS**

Daily application of 5 ml of a suspension containing 8.0 per cent monosodium cyanurate, 5 days per week for 3 months, to approximately 10 per cent of the body surface produced no local irritation but slight dilation of the Bellini's ducts. A 0.8 per cent suspension of the same compound and a 333 mg per liter solution of sodium dichloroisocyanurate produced no adverse effects. No irritation on the intact skin was observed after application of sodium (potassium) dichloroisocyanurate or trichloroisocyanuric acid in the form of dry powder for 24 hr. No

No eye damage or irritation was caused by the daily instillation of 0.1-ml suspension of 8 per cent monosodium cyanurate<sup>2 3</sup> or 333-ppm solution of sodium dichloroisocyanurate<sup>2 4</sup> in one eye of each of five animals 5 days per week for 3 months. No significant irritation was reported when one eye was exposed to a solution of potassium dichloroisocyanurate (3 ppm as available chlorine) flowing at approximately 330 ml per hr, 1 hr per day, 5 days per week, for a total of 30 exposures.<sup>30</sup>

# **TESTS ON HUMAN SUBJECTS**

The immersion of the entire forearms of 10 individuals in a neutralized trichloroisocyanuric acid solution (100 mg per liter as available chlorine) 8 times daily for 7 days caused no irritation. When the procedure was repeated for an additional 7 days, after a 2-week rest period, no evidence of sensitization was detected.<sup>30</sup>

# Discussion

#### Effect on Chlorine's Bactericidal Action

In laboratory experiments with buffered distilled water, cyanuric acid and cyanurates decrease the bactericidal activity of chlorine. However, adequate disinfection may be obtained by increasing the free available chlorine concentration to 1.0—1.5 mg per liter. The bactericidal activity of chlorinated isocyanurates in relation to hypochlorite on the basis of free available chlorine varies somewhat with the test organism used.

Results of field investigations are often inconclusive or even contradictory; cyanuric acid and cyanurates appear as both inhibitors and activators of chlorine as a bactericide. These contradictions, which may result from poor control of experimental conditions or from unknown chemical factors, remain to be explored in carefully designed

<sup>\*</sup> Commercial product containing 74.2 per cent active chlorine.

laboratory-field studies. In particular, the effect of pH in the presence of cyanuric acid should be investigated, since pools operated at a pH higher than 7.7 have shown an unsatisfactory disinfection record, even though the free chlorine concentration was kept in the range of 1.0—1.5 mg per liter.

# Carcinogenic Effects

The investigations conducted by Pliss and Zabezhinskii<sup>25</sup> with cyanuric acid may indicate a low carcinogenic potential. However, apparently these experiments were not adequately controlled, and the incidence of tumors observed might not be related to the compound tested. In addition, the subcutaneous route of application and the use of oil and benzene hardly reproduce the mode and form of entry under swimming pool conditions. Additional adequate tests\* are needed, since many persons of all ages might be exposed to this compound for a significant part of their lives. Chlorinated isocyanurates should also be tested. (For general criteria of carcinogenic studies, see Reference 31.)

#### Other Desirable Studies

#### **EMBRYOTOXIC EFFECTS**

Possible teratogenic and mutagenic effects of chlorinated isocyanurates should be assessed.

# CHRONIC TOXICITY OF TRICHLOROISOCYANURIC ACID

This compound should be tested in long term experiments to assess its chronic oral and dermal toxicity and its effect on eyes. The results of the 1-month toxicity studies on rats<sup>29</sup> should be considered with caution, as considerable decomposition of the compound with appreciable loss of active chlorine might have occurred during storage and administration of the experimental solutions. In fact, about 6 per cent and 31 per cent loss of available chlorine were found respectively in 0.2 per cent and 1.0 per cent (as available chlorine) solutions, pH 6.8–7.2, stored at 75–80°F for 6 hr.6

# POSSIBLE SYNERGISM

A direct investigation of the toxicity of combinations of chlorine (or chlorinated isocyanurates) and cyanuric acid is also desirable in order to assess a possible synergism.

#### **DERMAL ABSORPTION**

Specific skin absorption measurements of these compounds should be performed, since topical absorption is the most probable route of entry under swimming pool conditions.

#### **ADDITIONAL TESTS**

Eventual decomposition products should be identified and tested for possible toxic effects. Products of reactions with other compounds present in swimming pool water should be similarly investigated.

# Recommendations for Use

If these products are found toxicologically safe for swimming pools, cyanuric acid concentrations of 20–25 mg per liter, pH 7.2–7.7, with free available chlorine concentrations in the range of 1.0–1.5 mg per liter may satisfy disinfection requirements. However, not only accidental deviations from these conditions, such as elevated pH, but also factors that vary from pool to pool may weaken the bactericidal properties of the system. Bacteriological examinations should therefore be performed regularly and frequently. In addition, as a precaution against unknown soluble decomposition products, the pool water should be replaced periodically.

# Summary

The literature on chemical and bactericidal properties and toxicity of cyanuric acid and chlorinated isocyanurates is reviewed. On the basis of the results of experiments apparently conducted without contemporary controls, a low blastomogenic action in rats and mice was attributed to the administration of cyanuric acid. This conclusion remains to be verified in adequately controlled tests. If cyanuric acid is pronounced toxicologically safe for application in swimming pool disinfection, free available chlorine and cyanuric acid concentrations of 1.0–1.5 mg per liter and 20–25 mg per liter, respectively, may be adequate in the pH range 7.2–7.7. Accurate pH control and frequent bacteriological examinations are recommended.

#### References

- Baskin, H. A. Production of Cyanuric Acid from Urea. U.S. Patent 3,236,845, 1966.
- Cignitti, M., and Paoloni, L. Tautomeric Forms of Oxy-Derivatives of 1,3,5-Triazine. I. Infrared Spectra. Rend. Ist. Super. Sanita 23:1037-1047, 1960.
- 3. Cignitti, M., and Paoloni, L. Tautomeric Forms of Oxyand Oxo-Derivatives of 1,3,5-Triazine. II. The Ultraviolet Absorption of 2,4,6-Trimethoxy-1,3,5-Triazine and 2,4,6-Trioxo-1,3,5-Trimethylhexahydrotriazine. Spectrochim. Acta 20:211-218, 1964.
- Cignitti, M., and Paoloni, L. Tautomeric Forms of Oxygenated Derivatives of 1,3,5-Triazine. IV. Electronic Structure of Trimethoxy-s-Triazine and Its Triamide Tautomeric Form. Gazz. Chim. Ital. 96:413-426, 1966.

<sup>\*</sup> Feeding and skin painting studies with monosodium cyanurate in rats and mice are in progress sponsored by Olin Corp., FMC Corp., and Monsanto Co. (Personal communication, J. F. McCarthy, FMC Corp., June 4, 1973.)

- 5. McBrayer, R. L., and Nichols, N. S. Preparation of Cyanuric Acid. U.S. Patent 3,336,309, 1967.
- 6. Nelson, G. D. Swimming Pool Disinfection with Chlorinated Isocyanurates. Monsanto Company Special
- Report 6862, 1967.
  7. Padgett, W. M., and Hamner, W. F. The Infrared Spectra of Some Derivatives of 1,3,5-Triazine. J. Am. Chem. Soc. 80:803-808, 1958.
- 8. Paoloni, L., and Tosato, M. L. Tautomeric Forms of Oxygenated Derivatives of 1,3,5-Triazines. III. Kinetics of the Tautomeric Rearrangement of 2,4,6-Trimethoxy-1,3,5-Triazine. Chim. Ann. (Rome) 54:897-922. 1964.
- 9. Smolin, E. M., and Rapoport, L. The Chemistry of Heterocyclic Compounds, s-Triazines and Derivatives, p. 33. Interscience Publishers, Inc., New York, 1959.
- 10. Laszlo, L. Trichlorocyanuric Acid Bleaching and Disinfecting Compositions. U.S. Patent 2,897,154, 1959.
- 11. Boitsov, E. N., and Finkel'Shtein, A. I. Spectrophotometric Analysis of Melamine and the Products of Its Hydrolysis: Ammeline, Ammelide and Cyanuric Acid. Zh. Analit. Khim. 17:748-750, 1962.
- 12. Masayoshi, T. Separation and Determination of Cyanamide Derivatives. X. Separation and Determination of Cyanomelamine, Guanylmelamine, and Cyameluric Acid and Accompanying Compounds. Kogyo Kagaku Zasshi 64:1456-1460, 1961.
- 13. Kazarnovskii, S. N., and Lebedev, O. I. Determination of Melamine and Cyanuric Acid. Tr. Gor'kovsk. Politekh. Inst. 11:52-55, 1955.
- 14. Harlow, G. A., and Morman, D. H. Automatic Ion Exclusion-Partition Chromatography of Acids. Anal. Chem. 36:2438-2442, 1964.
- 15. Robinton, E. D., and Mood, E. W. An Evaluation of the Inhibitory Influence of Cyanuric Acid upon Swimming Pool Disinfection. Am. J. Public Health 57:301-310, 1967.
- 16. Stuart, L. S., and Ortenzio, L. F. Swimming Pool Chlorine Stabilizers. Soap Chem. Spec. 40:79-82, 1964.
- 17. Kowalski, X., and Hilton, T. B. Comparison of Chlorinated Cyanurates with Other Chlorine Disinfectants. Public Health Rep. 81:282-288, 1966.
- 18. Swatek, F. E., Raj, H., and Kalbus, G. E. A Laboratory Evaluation of the Effect of Cyanuric Acid on the Bactericidal Activity of Chlorine in Distilled Water and Seven Swimming Pool Water Systems. Paper presented at National Swimming Pool Institute Convention, January 21, 1967, Las Vegas, Nevada. Cited by Nelson.
- 19. Donohue, G. B., and Mulligan, J. F. 1970 Field Study of Cyanuric Acid as Applied to Swimming Pool Disinfection, Official Report of the Nassau County Department of Health, Mineola, New York, 1971.

- 20. Fitzgerald, G. P., and DerVartanian, M. E. Factors Influencing the Effectiveness of Swimming Pool Bactericides. Appl. Microbiol. 15:504-509, 1967.
- 21. Mazaev, V. T. Maximum Permissible Concentration of Cyanuric Acid and Its Monosodium Salt in Water Supplies. Gig. Sanit. 27:13-19, 1962.
- 22. Mazaev, V. T. Experimental Determination of the Maximum Permissible Concentrations of Cyanuric Acid, Monosodium Salt of Cyanuric Acid, Simazine, and a 2-Hydroxy Derivative of Simazine in Water Reservoirs. Sanit. Okhr. Vodoemov Zagryazneniya Prom. Stochnymi Vodami. 6:229—250, 1964.
- 23. Hodge, H. C., Panner, B. J., Downs, W. L., and Maynard, E. A. Toxicity of Sodium Cyanurate. Toxicol. Appl. Pharmacol. 7:667-674, 1965.
- Hodge, H. C. Studies of the Toxicity of Sodium Dichloroisocyanurate and of Monosodium Cyanurate. Food Machinery and Chemical Corp., 1959.
- 25. Pliss, G. B., and Zabezhinskii, M. A. Carcinogenic Properties of s-Triazine Derivatives. Vopr. Onkol. 16:82-85, 1970.
- 26. Haley, S. Teratogenic Study with Monosodium Cyanurate in Albino Rats. Report B758a to FMC Corporation from Industrial Bio-Test Laboratories. Inc., Northbrook, Ill., 1972.
- 27. Haley, S. Teratogenic Study with Monosodium Cyanurate plus chlorine in Albino Rats. Report B758c to FMC Corporation from Industrial Bio-Test Laboratories, Inc., Northbrook, Illinois, 1972.
- 28. Arnold, D. Mutagenic Study with Monosodium Cyanurate and Calcium Hypochlorite in Albino Mice. Report E756 to FMC Corporation from Industrial Bio-Test Laboratories, Inc., Northbrook, Illinois, 1972.
- 29. Hodge, H. C. One Month Studies of Rats Given Drinking Water Containing CDB-60, CDB-85, Cyanuric acid or Clorox. Report to FMC Corporation from the Division of Pharmacology and Toxicology of the University of Rochester, School of Medicine and Dentistry, Rochester, New York, 1958.
- 30. FMC Corporation, Inorganic Chemicals Division, technical data.
- 31. Food Protection Subcommittee on Toxicology, Food and Nutrition Board, Division of Biology and Agriculture, National Research Council. Evaluating the Safety of Food Chemicals. National Academy of Sciences, Washington, D.C., 1970.

#### **ACKNOWLEDGMENTS**

I would like to express my appreciation to Dr. G. Wolfgang Fuhs, Dr. William B. Lawson, and Dr. Douglas Mitchell of our Division and to Dr. Robert F. Korns of the Bureau of Cancer Control, New York State Department of Health, for their advice and cooperation.